Zoster Vaccines Session: Introduction of the Evidence to Recommendations Framework for Use of Recombinant Zoster Vaccine in Immunocompromised Adults

ACIP Meeting

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Background

- Risk of herpes zoster (HZ), severe disease, and complications generally higher in immunocompromised (IC) populations
- IC populations are very heterogeneous, both within and across groups
- Zostavax, a live, attenuated HZ vaccine, was contraindicated for persons with IC conditions
- Recombinant zoster vaccine (RZV, Shingrix) can potentially address need in IC populations

How many IC persons in the United States?*

- **~7 million IC adults[1]**
- **~3 million among:**
  - Hematopoietic stem cell transplant patients[2]
  - Patients with hematologic malignancies[3]
  - Renal or other solid organ transplant recipients[4]
  - Patients with solid tumor malignancies[3,5]
  - Individuals living with HIV[6]
- **~22 million with autoimmune and/or inflammatory (AI) conditions[7]**
  - >80 diverse conditions (e.g., systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease)
  - Often have underlying immune defects, but generally not considered frankly IC unless iatrogenic (i.e., on IC treatments)

*References on slide 18

Current ACIP Recommendations

- **ACIP recommended RZV in October 2017 for use in immunocompetent adults aged ≥50 years**
- **Immunocompromised persons:**
  - ACIP recommends use of RZV in persons
    - Taking low-dose immunosuppressive therapy
    - Anticipating immunosuppression or who have recovered from an immunocompromising illness
  - Because IC persons and those on moderate to high doses of immunosuppressive therapy were excluded from RZV efficacy studies, ACIP has not made recommendations on use of RZV in these patients

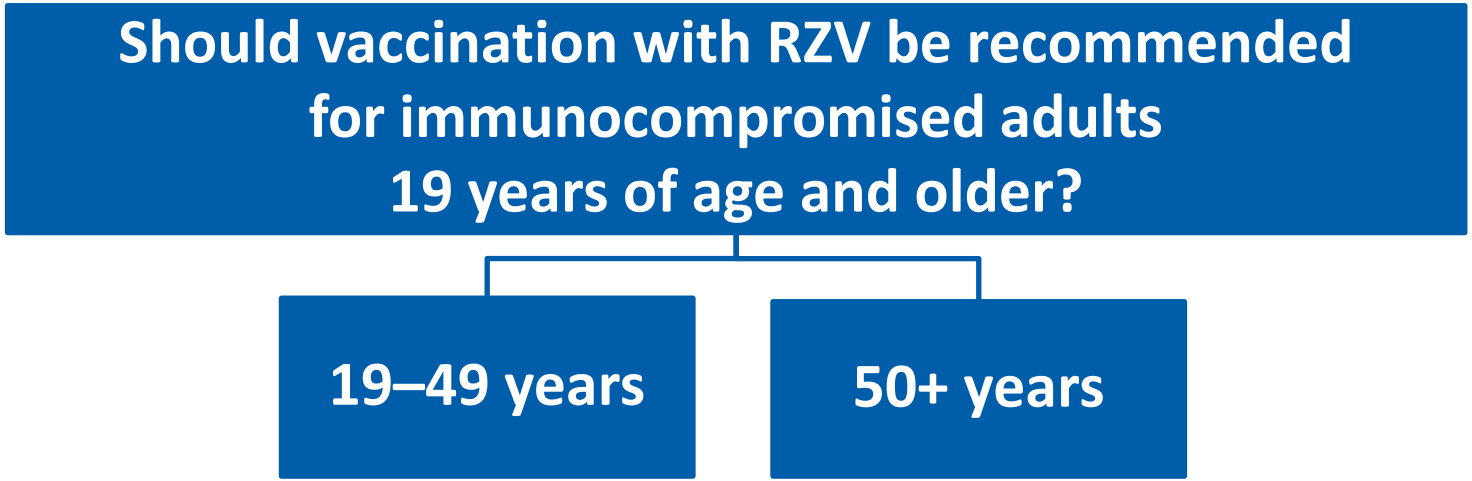
Dooling et al. Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines. MMWR Morb Mortal Wkly Rep 2018;67:103–108. DOI: http://dx.doi.org/10.15585/mmwr.mm6703a5.

RZV Updates

- **European Medicines Agency approved an expanded indication on August 25, 2020**
  - Shingrix now approved in the European Union for prevention of herpes zoster (HZ) and postherpetic neuralgia (PHN) in adults 50 years of age or older, and adults 18 years of age or older at increased risk of HZ
    - https://www.ema.europa.eu/en/medicines/human/EPAR/shingrix#assessment-history-section
- **Supplemental biologics license application submitted to FDA to support use in immunocompromised adults 18 years of age or older**
  - https://www.gsk.com/media/6189/q3-2020-results-announcement.pdf

Evidence to Recommendations (EtR) Framework:
Policy Question

- **Plan to split the policy question into two parts**



EtR Framework:
PICO Question

- **Population:** Immunocompromised adults ≥19 years of age
- **Intervention:** RZV, 2 doses at least 4 weeks apart
- **Comparison:** No vaccine
- **Outcomes**

Benefits		Harms	
Prevent HZ	**Critical**	**Serious adverse events**	**Critical**
Prevent PHN Prevent HZ-related hospitalization	Important	Immune-mediated disease Reactogenicity (Grade 3) Graft versus host disease (HSCT) Graft rejection (SOT)	Important

Immunocompromised Populations under Consideration

1. **Hematopoietic stem cell transplant patients (HCT)**
2. **Patients with hematologic malignancies (HM)**
3. **Renal or other solid organ transplant recipients (SOT)**
4. **Patients with solid tumor malignancies (STM)**
5. **Individuals living with HIV**
6. **Patients with primary and acquired immunodeficiencies or immunosuppression not covered in groups 1 through 5** (e.g., AI conditions)

EtR Framework

EtR Domain	Question
Public Health Problem	Is the problem of public health importance?
Benefits and Harms	How substantial are the desirable anticipated effects?
	How substantial are the undesirable anticipated effects?
	Do the desirable effects outweigh the undesirable effects?
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?
	Is there important variability in how patients value the outcomes?
Acceptability	Is the intervention acceptable to key stakeholders?
Feasibility	Is the intervention feasible to implement?
Resource Use	Is the intervention a reasonable and efficient allocation of resources?
Equity	What would be the impact of the intervention on health equity?

Public Health Importance:
Risk of HZ in IC Groups 1–5

- **Median HZ incidence estimates for these IC groups exceeded those reported for immunocompetent adults aged >50 years**
  - Variation in study estimates for cumulative incidence and incidence of HZ within each IC group
- **HZ complications and severe disease**
  - Increased in IC populations
  - Data insufficient to assess risk by group

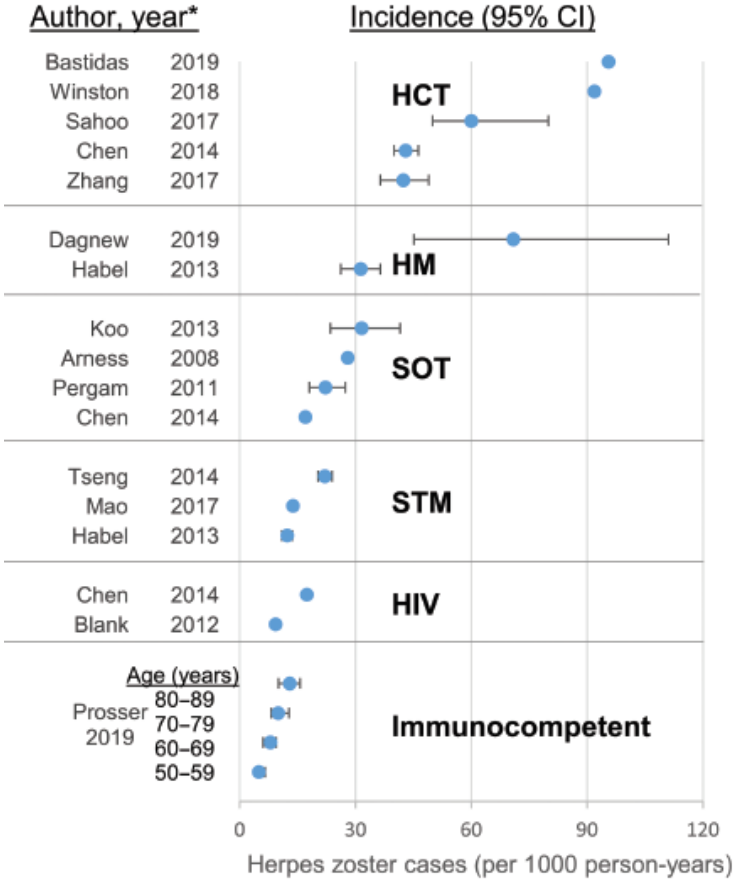


Figure 3. Herpes zoster incidence rates among patients with selected immunocompromising conditions. *Studies with low or medium risk of bias.

McKay et al. Herpes Zoster Risk in Immunocompromised Adults in the United States: A Systematic Review. CID 2020;71(7):e125–34.

Public Health Importance:
Risk of HZ in IC Group 6 (Figure: AI Conditions)

- **~1.5 to 2.0-fold higher risk in patients with AI conditions than in healthy individuals**
- **Risk varied across conditions and by age groups**
- **Age-standardized HZ incidence rates varied**
  - 19.9 per 1,000 person-years (SLE)
  - 6.8 per 1,000 person-years (gout)

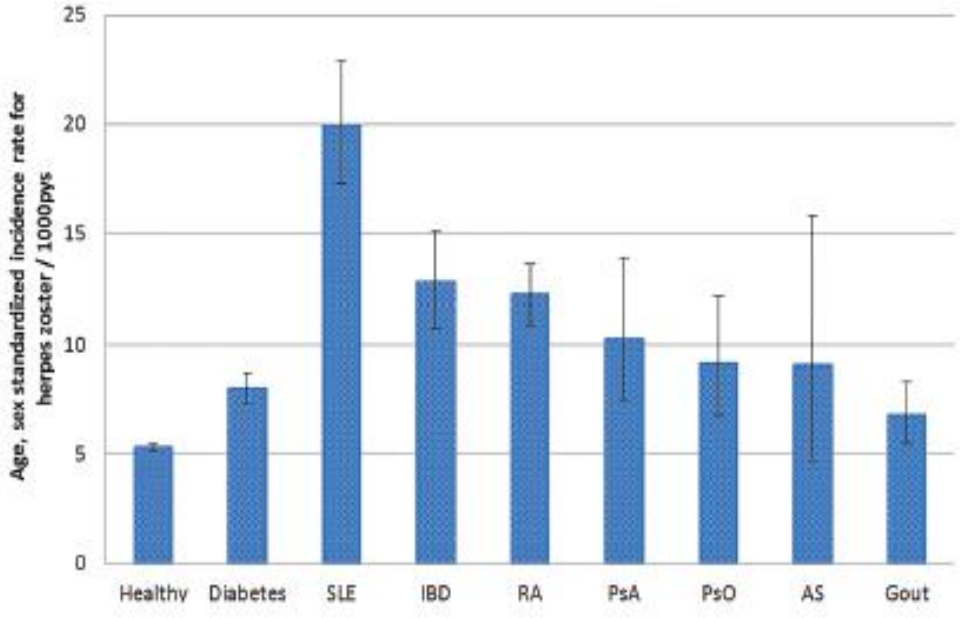


Figure 3. Age- and sex-standardized incidence rates (IRs)of HZ per 1,000 person-years, standardized to the values in the 2010 US Census population, among adults ages ≥20 years. Bars show the IRs of HZ with 95% confidence intervals. Cohorts of healthy adults without autoimmune diseases or diabetic conditions and adult patients with diabetes were used as controls. SLE=systemic lupus erythematosus; IBD=inflammatory bowel disease; RA=rheumatoid arthritis; PsA=psoriatic arthritis; PsO=psoriasis; AS=ankylosing spondylitis.

Yun et al. Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases. Arthritis & Rheumatology 2016;68(9):2328-2337.

Work Group Interpretation

- **Are HZ and HZ complications in IC adults of public health importance?**
  - Yes
- **Summary of work group discussions**
  - IC populations are very heterogeneous, both across and within groups
  - Risk of HZ and HZ complications generally higher in IC populations, although there is variability across and within IC groups
  - Not feasible to define every possible IC condition/medication combination
  - Important to consider broad recommendations and appropriate guidance for IC populations

EtR Framework:
Next Steps

- **Presentation on HZ in IC adults planned for next ACIP meeting**
- **Review available evidence regarding use of RZV in IC adults to address remaining EtR domains**
  - Benefits and Harms
  - Values
  - Acceptability
  - Feasibility
  - Resource Use
  - Equity

EtR Framework:
Next Steps, cont.

- **Review knowledge, attitudes, and practices**
- **GRADE analysis**
- **Cost effectiveness analysis of use of RZV in IC populations**
- **Update EtR Framework**

Question for ACIP

- **Do ACIP members have any questions or feedback regarding the initial EtR Framework for use of RZV in IC adults?**

Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Backup slides

Slide 3 References

1. Harpaz R, Dahl RM, Dooling KL, JAMA, 2016, 316(23):2547-8.
2. D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2018. Available at https://www.cibmtr.org.
3. American Cancer Society, https://cancerstatisticscenter.cancer.org; 2019 incidence estimates.
4. United Network for Organ Sharing, https://unos.org/data/transplant-trends/#transplants_by_organ_type+year; 2018, Renal= Kidney + Kidney/Pancreas, Solid organ = all listed.
5. Halpern MT, Yabroff KR, Cancer Invest, 2008, 26(6):647-51; Derived from Halpern and Yabroff 2000-2004 data on chemo/radiotherapy among all patients with cancers, adjusted based on proportion of all cancers in 2007 due to solid organ cancers, further adjusted by projections that solid cancers increased by 20% between 2007 and 2018 (data from American Cancer Society website).
6. CDC, https://www.cdc.gov/hiv/statistics/overview/ataglance.html; 2017 incidence, 2016 prevalence of diagnosed HIV infections.
7. Derived from Hayter SM. Autoimmun Rev. 2012 Aug;11(10):754-65 (prevalence 4.5% for all conditions excluding psoriasis) and Rachakonda TD. J Am Acad Dermatol. 2014 Mar;70(3):512-6 (prevalence of 3.2% for psoriasis alone), applied to projected adult US population in 2020 (US Census: 289.6 million).

IC Populations: Groups 1–5

IC Condition	Incident Cases (New cases per year)	Prevalent Cases
Hematopoietic stem cell transplant[1]	23,379	
Hematologic malignancy[2]	~176,200	
Solid organ (including renal) transplant[3]	58,532	~591,000
Solid tumor on chemotherapy[2,4]	~1,200,000	
HIV infection[5]	38,739	1,008,929
Total	~1,496,850	~1,599,929

1. D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2018. Available at https://www.cibmtr.org.
2. American Cancer Society, https://cancerstatisticscenter.cancer.org; 2019 incidence estimates.
3. United Network for Organ Sharing, https://unos.org/data/transplant-trends/#transplants_by_organ_type+year; 2018, Renal= Kidney + Kidney/Pancreas, Solid organ = all listed.
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